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(54) Title: PROCESS FOR CONCENTRATING A STERILANT AND STERILIZING ARTICLES THEREWITH

(57) Abstract

The present invention relates to a process for sterilization of medical instruments by concentrating a sterilant such as hydrogen peroxide inside of a sterilization chamber and sterilizing articles therewith. The sterilant is concentrated by removing more water from the sterilization chamber than peroxide.

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PROCESS FOR CONCENTRATING A STERILANT AND STERILIZING ARTICLES THEREWITH

FIELD OF THE INVENTION

The present invention relates to a process for sterilization of medical instruments using a chemical sterilant. More particularly, the invention relates to a process in which sterilization is achieved by concentrating a sterilant such as hydrogen peroxide inside of a sterilization chamber and sterilizing articles therewith.

BACKGROUND OF THE INVENTION

Medical instruments have traditionally been sterilized using either heat, such as is provided by steam, or a chemical, such as formaldehyde or ethylene oxide in the gas or vapor state. Each of these methods has its drawbacks. Many medical devices such as fiberoptic devices, endoscopes, power tools, etc., are sensitive to heat, moisture or both. Formaldehyde and ethylene oxide are both toxic gases that pose a potential hazard to healthcare workers. Problems with ethylene oxide are particularly severe, because its use requires long aeration times to remove the gas from articles that have been sterilized. This lengthens the sterilization cycle time undesirably.

Sterilization using liquid hydrogen peroxide solution has been found to require high concentrations of sterilant, extended exposure time and/or elevated temperatures. However, sterilization using hydrogen peroxide vapor has been shown to have some advantages over other chemical sterilization processes (see, e.g., U.S.

Patent Nos. 4,169,123 and 4,169,124, each of which issued September 25, 1979, which are entitled respectively, "Hydrogen Peroxide Vapor Sterilization Method" and "Cold Gas Sterilization Process" and which are incorporated herein by reference).

The combination of hydrogen peroxide with a plasma provides certain additional advantages, as disclosed in U.S. Patent No. 4,643,876 issued February 17, 1987 and entitled, "Hydrogen Peroxide Plasma Sterilization System" which is incorporated herein by reference. Commercially available sterilization devices, such as the STERRAD® sterilization systems sold by Advanced Sterilization Systems division of Ethicon, Inc. automate the process of injecting a solution of hydrogen peroxide into a sterilization chamber, vaporizing the solution to provide a hydrogen peroxide vapor, contacting articles to be sterilized with the vapor, and exciting the vapor into the plasma stage. The hydrogen peroxide for each sterilization cycle is shipped to the location of the sterilization system, generally by air or ground transportation.

Preferably, as in the case with the STERRAD® brand systems, pre-measured amounts of a hydrogen peroxide and water solution are provided in sealed enclosure, such as a capsule inside of a cassette housing which can be automatically opened by the system to reduce contact between the system user and the hydrogen peroxide solution. Such cassettes are described more fully in U.S. Patent No. 4,817,800 issued April 4, 1989 entitled, "Fluid Injection System Cassette and Fluid Packaging Methods" and U.S. Patent No. 4,899,519 issued February 13, 1990 with the same title, each of which are incorporated herein by reference.

The sterilization of articles containing diffusion-restricted areas, such as long narrow lumens, presents a special challenge. Methods that use hydrogen peroxide

vapor that has been generated from an aqueous solution of hydrogen peroxide have certain disadvantages. One disadvantage is that because water has a higher vapor pressure than hydrogen peroxide, it will vaporize faster. Another disadvantage is that because of its lower molecular weight, water will diffuse faster than hydrogen peroxide in the vapor state. Because of these physical properties, when an aqueous solution of hydrogen peroxide is vaporized in the area surrounding the items to be sterilized, the water reaches the items first and in higher concentration. The water vapor more quickly diffuses into and thus inhibits penetration of hydrogen peroxide vapor into diffusion-restricted areas, such as small crevices and long narrow lumens. Simply employing a more concentrated solution of hydrogen peroxide fails to adequately address the problem due to the difficulty in handling highly concentrated hydrogen peroxide solutions. Transportation of such solutions can be particularly difficult. In general, such solutions are limited to concentrations of less than 60% hydrogen peroxide, however, regulations and the like regarding such concentrations may of course be modified in the future. In any event, shipping and handling of highly concentrated solutions remains impractical.

U.S. Patent No. 4,952,370 issued August 28, 1990 and entitled "Hydrogen Peroxide Sterilization Method" and incorporated herein by reference discloses a sterilization process in which aqueous hydrogen peroxide vapor is first condensed on the article to be sterilized, followed by application of a vacuum to the sterilization chamber to remove the water and hydrogen peroxide from the article. This method is suitable for surface sterilization, but not for sterilization of diffusion-restricted areas such as long narrow lumens because it depends on the diffusion of hydrogen peroxide vapor into the lumen to effect sterilization.

U.S. Patent No. 4,943,414 issued July 24, 1990 and entitled "Method for Vapor Sterilization of Articles Having Lumens" discloses a process in which a

vessel containing a small amount of a vaporizable liquid sterilant solution is attached to a lumen, and the sterilant vaporizes and flows directly into the lumen of the article as the pressure is reduced during the sterilization cycle. This system has the advantage that the water and hydrogen peroxide vapor are pulled through the lumen by the existing pressure differential, increasing the sterilization rate for lumens, but has the disadvantage that the vessel needs to be attached to each lumen to be sterilized.

U.S. Patent No. 5,492,672 issued February 20, 1996 and entitled, "Sterilization Apparatus and Method for Multicomponent Sterilant" discloses a process for sterilizing narrow lumens. This process uses a multi-component sterilant vapor and requires successive alternating periods of flow of sterilant vapor and discontinuance of such flow. A complex apparatus is used to accomplish the method. Because flow through of vapor is used, closed end lumens are not readily sterilized in the process.

U.S. Patent No. 4,744,951 issued May 17, 1988 to Cummings and entitled "Vaporization method to Enhance Sterilant Penetration" attempts to address this problem by providing a separate prechamber connected to the sterilization chamber. Hydrogen peroxide is first admitted to the prechamber where it is concentrated in a distillation procedure employing the differing vapor pressures of hydrogen peroxide and water. Water's higher vapor pressure allows one to select a vaporization pressure that selectively vaporizes water from a hydrogen peroxide solution, thus concentrating the solution. Cummings pumps air out of the prechamber and lowers its pressure to a level at which the water preferentially vaporizes from the hydrogen peroxide solution. The pump that is evacuating the prechamber draws out the water vapor thus released from solution to concentrate the remaining solution. To prevent the water vapor from traveling into the narrow spaces such as endoscope lumens,

Cummings carries out the concentration process in the prechamber which is physically isolated from the main chamber. This adds complexity by requiring additional chambers, pumps and valves.

Those of skill in the art would not think to employ such a concentration process in the same chamber as the sterilization occurs. Such a process first draws the water out of solution and it would have been thought that this water vapor would simply enter and thus occlude the narrow lumens, thereby inhibiting the later diffusion of hydrogen peroxide, no matter how concentrated, into those lumens. However, the present inventors have surprisingly found that concentrating the hydrogen peroxide vapor within the sterilization chamber greatly increases the ability to sterilize long narrow lumens over the conventional process.

SUMMARY OF THE INVENTION

One aspect of the present invention comprises a method of furnishing concentrated hydrogen peroxide vapor to an article. It includes the following steps:

placing the article into a chamber containing an inner atmosphere;

placing a solution comprising hydrogen peroxide and water into fluid communication with the chamber, the solution having a ratio of hydrogen peroxide to water;

vaporizing the solution in the inner atmosphere to form water vapor and hydrogen peroxide vapor;

selectively drawing water vapor from the chamber to increase a ratio of hydrogen peroxide to water in the chamber; and

contacting the article with the hydrogen peroxide vapor.

Preferably, the ratio of hydrogen peroxide vapor to water vapor after the step of selectively drawing water vapor from the chamber exceeds the ratio of hydrogen

peroxide to water in the solution. Preferably, the ratio of hydrogen peroxide to water, by weight, after the step of selectively drawing water vapor from the chamber exceeds 3 to 1, more preferably 4 to 1; and the ratio of hydrogen peroxide to water in the solution, by weight, is preferably less than 3 to 1, more preferably less than 3 to 2.

The step of selectively drawing water vapor from the chamber preferably comprises placing the solution within a diffusion restricted environment in fluid communication with the chamber during the step of vaporizing the solution; the diffusion restricted environment is preferably more diffusion restricted during the step of selectively drawing water vapor from the chamber than during a portion of the step of vaporizing the solution without selectively drawing water vapor from the chamber.

In one aspect of the invention the water vapor is drawn from the chamber through one or more exhaust ports and wherein the one or more exhaust ports are physically remote from the diffusion restriction.

Preferably, the temperature and pressure of the solution are controlled during the step of vaporizing the solution to enhance vaporization of the water from solution versus vaporization of hydrogen peroxide to thus extract at least a portion of the water vapor from the chamber.

One aspect of the invention comprises maintaining the solution at a pressure below the vapor pressure of the water in the solution and above the vapor pressure of the hydrogen peroxide in the solution while selectively drawing water vapor from the chamber. To increase the vapor pressure of the water in the solution relative to the hydrogen peroxide in the solution and thus enhancing the ability to selectively

vaporize and extract the water vapor, the temperature of the solution can be held below the temperature of the atmosphere in the chamber. For instance, the temperature of the atmosphere in the chamber can be above room temperature and the temperature of the solution during the vaporizing step can be held at least 10° C below the temperature of the atmosphere in the chamber. One way to achieve this is to thermally isolate the vaporizer from the chamber. y isolated from the chamber.

In one aspect of the invention, the temperature and pressure of the solution are controlled during a least a first portion of the vaporizing step so as to selectively vaporize water from the solution and concentrate hydrogen peroxide therein to form a concentrated solution and during a second portion of the vaporizing step the temperature of the concentrated solution is raised and then vaporized. Preferably, after the solution is concentrated, no more atmosphere is evacuated from the chamber so as to conserve hydrogen peroxide.

Preferably, the chamber is dried prior to vaporizing the solution, such as by pumping a portion of the atmosphere out of the chamber or by applying energy to excite molecules of liquid water within the chamber into the gaseous or plasma state of matter and pumping a portion of the atmosphere out of the chamber.

In one aspect of the invention, the step of contacting the article with the hydrogen peroxide vapor is limited to less than one hour and if the article were to have a straight round lumen having two open ends, a diameter of 1mm and a length of 250mm with 10^6 viable spores of B. Stearothermophilus located within the lumen at a midpoint thereof, all of the spores would be killed.

In one aspect of the invention the solution comprises peracetic acid.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a schematic diagram of a chamber and accessories suitable for use in the hydrogen peroxide sterilization process of the invention.

FIG. 2 is a schematic diagram of a chamber, pump and throttle valve for use in the hydrogen peroxide sterilization process of the invention.

FIG. 3 is a schematic diagram of a system with one pump and two valves, one valve having a larger pump vacuum line for quicker pumpdown and one having a smaller vacuum line for slower pumpdown.

FIG. 4 is a schematic diagram of a single valve sterilization system having two pumps, one for slower pumpdown and one for quicker pumpdown.

FIG. 5 is a schematic diagram of a system with two pumps and two valves, one pump for slower pumpdown and one for quicker pumpdown.

FIG. 6 is a schematic diagram of a system with a vaporizer.

FIG. 7 is a schematic diagram of a system with an alternative vaporizer.

FIG. 8 is a schematic diagram of a system with a further alternative vaporizer.

FIG. 9 is a graph showing the pressure and peroxide concentration during a concentrating process.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Sterilizing the inside of lumened devices has always posed a challenge to sterilization systems. Co-pending U.S. Application No. 08/628,965, and its related issued U.S. Patent No. 5,980,825 issued November 9, 1999, the entire contents of which are hereby incorporated by reference, disclose a method of hydrogen peroxide vapor sterilization of diffusion-restricted environments, such as long narrow lumens, at pressures less than the vapor pressure of hydrogen peroxide by pretreating the article to be sterilized with a dilute solution of hydrogen peroxide prior to exposure

to a vacuum. U.S. Patent 5,851,485, issued December 22, 1998 incorporated herein by reference, controls the pumpdown rate.

An apparatus useful in the process of the present invention is shown schematically in FIGS. 1 and 2 and comprises a chamber 2, a throttle valve 4 and a pump 6. In FIG. 2, the chamber 2 is attached to the pump 6 by the throttle valve 4. The valve 4 can be controlled either automatically or manually to maintain the pressure. In the automatic mode of operation, the throttle valve 4 opens based on the pressure in the chamber via a pressure transducer and valve controller. Such valves are commercially available from, for example, MKS (Andover, MD).

Hydrogen peroxide can be introduced into the system in any fashion. In one embodiment, a dilute, aqueous solution of hydrogen peroxide is placed in wells 8 as shown in FIG. 1. The aqueous solution of hydrogen peroxide can also be placed within the lumen of long narrow objects to be sterilized. As the pressure in the sterilization chamber 2 is reduced, the hydrogen peroxide vaporizes and contacts the surface to be sterilized (i.e., colonoscope 10 in FIG. 1) which is placed on metal grid 12 which rests on tray 14. In a preferred embodiment, the tray can be configured with a plurality of wells designed to retain a known volume of liquid sterilant. In one embodiment, the volume of sterilization chamber 2 is about 18.5 liters and its dimensions are about 22" (55.9 cm) × 4.25" (10.8 cm) × 12" (30.5 cm).

FIG. 3 illustrates a parallel two-valve arrangement for use in the sterilization process of the invention. In this embodiment, the chamber 2 is in fluid communication with the pump 6 via valves 16 and 18. Valve 16 mediates the initial rapid evacuation, the first step of a two step evacuation process. Valve 18 mediates slow evacuation, the second step of the process, which ensures maximal contact of the article to be sterilized with the vaporized aqueous hydrogen peroxide. The

pumpdown rate can be controlled by the pumping speed and/or the percent opening of the valve. Either valve can be used to maintain the pressure. In practice, controlling the process so that all of the water evaporates before any of the hydrogen peroxide evaporates is very difficult, yet the preferential evaporation and elimination of water vapor from the system effectively concentrates the hydrogen peroxide therein without the attendant complexity of shipping and handling concentrated hydrogen peroxide solutions prior to vaporization.

As the water evaporates from the solution, its molecules in the vapor state greatly increase thus raising the pressure in the system and requiring additional pumping to extract the water vapor to maintain the pressure between the two vapor pressures. Also, the vapor pressures change with changing conditions within the chamber.

FIG. 4 illustrates a sterilization apparatus having two pumps 20 and 22, and one valve 4. Pump 20 allows quicker pumpdown of the chamber 2, while pump 22 allows slower pumpdown. FIG. 5 illustrates an alternate configuration having two valves 24 and 26 in fluid communication with the pumps 20 and 22, respectively.

Regardless of which configuration is used, hydrogen peroxide can be introduced into the chamber as a liquid. In one preferred embodiment, hydrogen peroxide is introduced as a vapor and the chamber parameters are changed so that the vapor condenses as a liquid on the surface of interior of an article to be sterilized. Such changes include increasing the pressure.

The aqueous solutions of hydrogen peroxide can be relatively dilute, e.g. as low as 1-6% peroxide by weight, since sterilization is not achieved through contact with the hydrogen peroxide solution, but rather is achieved at low temperatures

(preferably 15°-80°C, more preferably 20°-60°C, still more preferably 40°-55°C) and in short periods of time (preferably less than one hour, and more preferably less than one-half hour) upon exposure to hydrogen peroxide under vacuum. The method of the present invention is particularly effective with articles having inaccessible or hard-to-reach places. Such articles include long, narrow lumens, hinges and other articles having spaces where diffusion of vapors is restricted. Although hydrogen peroxide is used in the examples described herein, the use of other liquid sterilants which have vapor pressures lower than the vapor pressure of the solvent in which they are provided are also contemplated. Such sterilants include, for example, aqueous peracetic acid solution and aqueous glutaraldehyde solution.

Preferably, the article to be sterilized is contacted with sterilant prior to the vaporization step to localize at least some of the vaporization in the diffusion restricted areas. Such contacting can be accomplished either directly or indirectly. Direct contacting includes methods such as static soaking, flow through, aerosol spray, condensation of a vapor. Any other methods involving physically contacting the articles to be sterilized with sterilant would be considered direct contacting. Indirect contacting includes those methods in which sterilant is introduced into the chamber, but not directly on or in the articles to be sterilized.

At the end of the process, deep vacuum can be used to remove residual sterilant. A plasma can also be used to both enhance sterilization efficacy and to remove residual sterilant.

The pumps shown schematically in the figures can be any commercially available vacuum pump. Two preferred pumps are from Leybold Vacuum Products, Inc. (Export, PA) (Model D16A, pump rate = 400 liters/min) and KNF Neuberger,

Inc. (Trenton, NJ, Model N740, pump rate = 45 liters/min). The Leybold pump can reach a pressure of less than 0.1 torr and the KNF pump can reach a pressure of less than 10 torr.

For certain substrates being sterilized, such as nylon or polyurethane, excess hydrogen peroxide in the system may leave a residual which is difficult to be removed. In order to avoid an excess residual, the vapor concentration of hydrogen peroxide is preferably kept below 30 mg/l, more preferably less than 20 mg/l, and more preferably still less than 15 mg/l. If higher vapor concentrations of hydrogen peroxide are desired, excess residual can be removed using a gas plasma. When using substrates such as stainless steel, polyethylene or polypropylene, which do not retain a residual, there is no reason to limit to the amount of peroxide which can be present in the vapor phase in the system during sterilization.

To further reduce water within the system, the chamber 2 may be dried prior to the introduction of hydrogen peroxide. Many means may be employed to drive water out of the chamber. Primarily, this is accomplished by vaporizing the water and pumping it out of the chamber. The vaporization can be accomplished with heat, plasma induction, vacuum or the like, either alone or in combination. Merely drawing a vacuum prior to introducing the hydrogen peroxide accomplishes a beneficial drying of the chamber 2. If the chamber 2 is heated during this process and if a high energy electromagnetic field is applied to urge the water into the plasma stage the drying is enhanced. U.S. Patent No. 5,656,238 issued on August 12, 1997 to Spencer at al. and incorporated herein by reference teaches such techniques in more detail.

Vaporization of the hydrogen peroxide can be achieved using well known methods as described above; FIGS. 6 to 8 show several new preferred methods. In

FIG. 6, a chamber 30 is evacuated by a pump 32 separated from the chamber 30 by a throttle valve 34. A vaporizer 36 comprises a housing 38 in fluid communication with the chamber 30 and into which extends a liquid feeding nozzle 40 from outside of the chamber 30. A cup 42 within the housing 38 receives hydrogen peroxide from the nozzle 40. The hydrogen peroxide can be vaporized as it exits the nozzle 40, or more preferably in a controlled fashion from the cup 42 by controlling the temperature of the cup 42 and the pressure in the chamber 30. Temperature control of the cup 42 can be as simple as thermally isolating it from the chamber 30, or a more active control system can be employed such a cooling coil or the like to maintain the cup 42 at a desired low temperature. Preferably, the entire vaporizer 36 is thermally isolated from the chamber 30 or temperature controlled in some fashion. Lower temperatures of vaporization enhance the preferential vaporization of water by exploiting the larger difference between the vapor pressures of water and hydrogen peroxide at lower temperatures. Creating a diffusion restriction 44 between the vaporizer 36 and chamber 30 enhances the preferential extraction of water vapor from the chamber as water vapor will more easily traverse the diffusion restriction and be pumped out of the chamber during the vaporization process. The diffusion restriction 44 may be simply reducing the clearance between the cup 42 and housing 38 through with the vapor must travel to reach the chamber 30.

FIG. 7 shows a similar chamber 50, pump 52 and valve 54 with modified vaporizer 56. The vaporizer 56 comprises a chamber 58 separated from the chamber 50 by a diffusion restriction 60, such as a permeable membrane. Liquid hydrogen peroxide solution enters the chamber 58 through a valve 62. FIG. 8 illustrates a similar arrangement with a chamber 70, pump 72, valve 74, and vaporizer 76 with a chamber 78 and valved hydrogen peroxide solution inlet 80. Restriction of the diffusion between the vaporizer chamber 78 and main chamber 70 is variable. During initial vaporization when primarily water is vaporizing the vapors pass

through a tight diffusion restriction 82. After the concentration of the hydrogen peroxide solution reaches a given level valve 84 may be opened to speed the vaporization and diffusion of the concentrated hydrogen peroxide solution.

Preferably, the temperature in the chamber is no less than 5°C nor more than 150° C, with the range of 40 to 60°C being preferred, and the pressure should be no less than 0.01 torr, nor typically greater than atmosphere during the process, with the lowest vacuum being typically 0.1 torr and the diffusion pressure preferably being between 1 and 15 torr, although other conditions within the spirit of the invention will be apparent to those of skill in the art. During the concentration stage, the pressure should not fall below 0.3 torr. Shorter overall cycles are preferred for convenience, with 5 minutes being a desirable goal, but longer times upwards of 6 hours or more may be warranted in some circumstances.

Tables 1 and 2 illustrate the effectiveness of the present invention. The experiments were run on a chamber of 73 liters at 45°C with 1480 mg of 59% hydrogen peroxide solution by weight. The vaporizer is separated from the chamber by twelve 2 mm diameter holes to effect diffusion restriction. Test A was conducted by opening the valve, evacuating the chamber to 0.3 torr, closing the valve, injecting the peroxide solution into the vaporizer, allowing the water and peroxide to vaporize and diffuse, and venting the chamber. Test B was conducted by injecting peroxide solution into the vaporizer at the atmospheric pressure, opening the valve, evacuating the chamber to 2 torr, closing the valve, allowing the remaining water and peroxide to vaporize and diffuse, and venting the chamber. Test C was conducted by opening the valve, evacuating the chamber, injecting the peroxide solution into the vaporizer when the chamber was evacuated to 30 torr, continuing to evacuate the chamber to 2 torr, closing the valve, allowing the remaining water and peroxide to vaporize and diffuse, and venting the chamber. The procedure for test D

was same as test C except the peroxide solution was introduced into the vaporizer at 0.3 torr. Test E was conducted by opening the valve, evacuating the chamber to 0.3 torr, closing the valve, injecting the peroxide solution into the vaporizer, allowing the water and peroxide to vaporize and diffuse for 30 seconds, opening the valve, evacuating the chamber to 2 torr, closing the valve, allowing the remaining water and peroxide to vaporize and diffuse, and venting the chamber.

Table 1

Step	Test conditions				
	Normal process	New concentrating Process			
	Test A	Test B	Test C	Test D	Test E
1	Open valve	Inject H_2O_2 at 1 atm	Open valve	Open valve	Open valve
2	Vacuum to 0.3 torr	Open valve	Vacuum to 30 torr	Vacuum to 0.3 torr	Vacuum to 0.3 torr
3	Close valve	Vaporization & diffusion	Inject H_2O_2 at 30 torr	Inject H_2O_2 at 0.3 torr	Close valve
4	Inject H_2O_2 at 0.3 torr	Vacuum to About 2 torr	Vaporization & diffusion	Vaporization & diffusion	Inject H_2O_2 at 0.3 torr
5	Vaporization & diffusion	Close valve	Vacuum to About 2 torr	Vacuum to About 2 torr	Vaporization & diffusion
6	Vent to 1 atm	Vaporization & diffusion	Close valve	Close valve	Open valve
7		Vent to 1 atm	Vaporization & diffusion	Vaporization & diffusion	Vacuum to About 2 torr
8			Vent to 1 atm	Vent to 1 atm	Close valve
9					Vaporization & diffusion
10					Vent to 1 atm

Table 2 shows the efficacy results with and without the concentrating process in the chamber. The tests were conducted by placing one stainless steel wire inoculated with $4.3x10^6$ Bacillus stearothermophilus spores at the center of the stainless steel lumen. Four 1 mm lumens with length ranging from 250 mm to 400 mm were used for each test. All the experiments were conducted by controlling the time between the injecting of peroxide solution and the venting of the chamber to 6 minutes. The results indicate that the new concentrating process is more efficacious than the normal process which does not concentrate the peroxide in the chamber. These results also indicate that the peroxide solution can be introduced before evacuating the chamber, during evacuating the chamber with pressure above or below the vapor pressure of peroxide, or after evacuating the chamber with the valve at the either open or closed position.

Table 2

	Sterility test result (positives / samples)				
	Normal process	New concentrating Process			
	Test A	Test B	Test C	Test D	Test E
1 x 400 mm	2 / 2	0 / 2	0 / 2	0 / 2	0 / 2
1 x 350 mm	2 / 2	0 / 2	0 / 2	0 / 2	0 / 2
1 x 300 mm	2 / 2	0 / 2	0 / 2	0 / 2	0 / 2
1 x 250 mm	2 / 2	0 / 2	0 / 2	0 / 2	0 / 2

Monitoring of the temperature, pressure and hydrogen peroxide conditions within the chamber 30 (FIG. 6) allows the process to be controlled more precisely. Preferably, an automated control system, preferably employing a computer processor, receives signals of the temperature, pressure and perhaps also the hydrogen peroxide concentration and calculates the optimal pressure at which to maintain the chamber to remove the water from the hydrogen peroxide solution and from the chamber 30. It can also determine when the solution is sufficiently concentrated. For instance, it may be desired to only concentrate the solution to a certain degree so as to minimize the loss of hydrogen peroxide from the chamber, thereby minimizing hydrogen peroxide emissions from the chamber. While preferentially vaporizing the water from the solution, some hydrogen peroxide will also vaporize. Accordingly, one may wish to balance the efficient use of the quantity of hydrogen peroxide within the solution against the goal of eliminating all water from the solution and the chamber. By monitoring the ratio of water to peroxide in the vapor phase, the valve 34 can be controlled to remove the vapor until the desired ratio is achieved. The ratio can be determined using a hydrogen peroxide monitor and a moisture monitor, or by using a hydrogen peroxide monitor and a pressure sensor and then calculating the water using the PV=nRT equation and making the assumption that water and peroxide are essentially the only gases within the chamber 30.

It is known that certain spectra of light passing through the chamber can be measured to determine the hydrogen peroxide concentration. One particular method is disclosed in co-pending U.S. Application No. 08/970,925 filed November 14, 1997, incorporated herein by reference.

Table 3 compares a sterilization process in which the concentration of hydrogen peroxide is not increased with a process in which it is increased according to

the present invention. The concentrations of water and peroxide for the normal process without concentrating the peroxide were calculated based on 1480 mg of 59% peroxide solution by weight in a 73 liters chamber. Test E procedure described in Table 1 was used to determine the concentrations of water and peroxide in the chamber with the concentrating process. The concentration of peroxide was measured with a peroxide monitor and the concentration of water was calculated from the pressure and peroxide monitor readings. Unlike the normal process which retains all the peroxide in the chamber, the concentrating process has less available peroxide in the chamber, but it removes more water than peroxide from the chamber and results in more concentrated peroxide for achieving better efficacy.

Table 3

	Normal process	New concentrating process
Concentration of water	8.3 mg/L	1.5 mg/L
Concentration of peroxide	12.0 mg/L	7.3 mg/L
Ratio of peroxide to water	1.45	4.87

Table 4 also illustrates effects of the ratio of hydrogen peroxide vapor to water vapor in the chamber 30 on the ability to sterilize long narrow lumens or other diffusion restricted environments with Bacillus subtilis var. niger spores on stainless steel blades in 3mm x 500 mm stainless steel lumen. Water vapor was first introduced into the system and then essentially pure hydrogen peroxide vapor was introduced by liberation from a solid form. The lower concentrations of water show no failures, whereas with the higher ratio in the last column the efficacy decreased and in one test 3 out of 3 samples failed. Therefore, it is desirable to control the amount of water and peroxide in the chamber to achieve better efficacy.

Table 4

	Sterility results (positives / samples)		
Diffusion time of peroxide (minutes)	0.653 mg/L water + 6 mg/L peroxide	3.266 mg/L water + 6 mg/L peroxide	6.532 mg/L water + 6 mg/L peroxide
5	0 / 3	0 / 3	3 / 3
10	0 / 3	0 / 3	2 / 3
15	0 / 3	0 / 3	0 / 3
30	0 / 3	0 / 3	0 / 3

Water vaporizes and diffuses faster than the peroxide under the same temperature and pressure conditions. At the beginning of the injection stage, the ratio of peroxide to water vaporized into the vapor phase is much lower than the ratio of peroxide to water in the liquid introduced into the vaporizer. By leaving the valve at the open position during the injection stage, more water can be removed from the chamber than the peroxide. As more water vaporized from the vaporizer and removed from the chamber, the peroxide concentration left in the system is increased. Table 5 shows the degree of concentration achieved according to the present invention by changing the pressure that the valve was closed during the concentrating process with the test E procedure described in Table 1. A total of 1480 mg of 59% by weight hydrogen peroxide solution was used for each test. The results indicate that water is removed faster than the peroxide from the system and the wt% of peroxide is increased by evacuating the system to a lower pressure.

Table 5

	Normal process	New concentrating process		
		Valve closed at 4 torr	Valve closed at 3 torr	Valve closed at 2 torr
Concentration of water	8.3 mg/L	3.5 mg/L (58% removed)	2.7 mg/L (67% removed)	1.5 mg/L (82% removed)
Concentration of peroxide	12.0 mg/L	10.5 mg/L (12% removed)	10.0 mg/L (17% removed)	7.3 mg/L (39% removed)
Ratio of peroxide to water	1.45 : 1 (59% by wt)	3.0 : 1 (75% by wt)	3.7 : 1 (79% by wt)	4.9 : 1 (83% by wt)

Table 6 discloses another approach to control this concentrating process by directly monitoring the ratio of peroxide to water in the chamber. The valve is then closed when the desired ratio of peroxide to water is reached.

Table 6

	Ratio of peroxide to water		
	Beginning of the injection stage	Right after concentrating	After all peroxide vaporized
Solution in the vaporizer	1.45 : 1	19 : 1	No solution left in the vaporizer
Vapor in the chamber	Very low	0.85 : 1	4.9 : 1

The test conditions described in Table 5 were repeated with 1780 mg of 59% peroxide solution by weight. Efficacy tests were also conducted under the same conditions with stainless steel wire inoculated with $4.3x10^6$ Bacillus stearothermophilus spores located at the center of the stainless steel lumen. The results, presented in Table 7, clearly indicate that the new concentrating process is more efficacious than the normal process to sterilize lumen devices and all lumens tested with the new concentrating process at three pressure levels were sterilized.

Table 7

	Normal process	New concentrating process		
		Valve closed at 4 torr	Valve closed at 3 torr	Valve closed at 2 torr
Concentration of peroxide	14.4 mg/L	6.41 mg/L	4.52 mg/L	3.17 mg/L
Efficacy with 1mm x 400mm SS lumen	2 / 2	0 / 2	0 / 2	0 / 2
Efficacy with 1mm x 350mm SS lumen	2 / 2	0 / 2	0 / 2	0 / 2
Efficacy with 1mm x 300mm SS lumen	2 / 2	0 / 2	0 / 2	0 / 2
Efficacy with 1mm x 250mm SS lumen	2 / 2	0 / 2	0 / 2	0 / 2

Table 8 shows the efficacy of the concentrating process with 12% peroxide solution by weight. Tests were conducted by placing one stainless steel wire inoculated with $2.1x10^6$ Bacillus stearothermophilus spores at the center of the stainless steel lumen. Four 1 mm lumens with length ranging from 250 mm to 400 mm were used for each test. The normal process was conducted by evacuating the chamber to 0.3 torr, closing the valve, injecting 7400 mg of 12% peroxide solution by weight into the vaporizer, allowing the water and peroxide to vaporize and diffuse for a total of 23 minutes, and venting the chamber. The concentrating process was conducted by evacuating the chamber to 0.3 torr, introducing 7400 mg of 12% peroxide solution by weight into the vaporizer with the valve at the open position, allowing the water and peroxide to vaporize and diffuse, closing the valve when the peroxide concentration increased to 0.45 mg/L, allowing the remaining water and peroxide to vaporize and diffuse, and venting the chamber. Due to the excess of the solution introduced into the vaporizer, the valve was remained at the open position for 16 minutes to remove enough water from the sterilizer and to concentrate the peroxide that remained in the system. The valve was then closed for an additional 7 minutes to allow the remaining peroxide to vaporize and diffuse. The total peroxide exposure time for both processes were 23 minutes. The results, as shown in the Table 8, indicate that the concentrating process is more efficacious than the normal process and diluted peroxide solution can also be used in this concentrating process. These results also indicate that monitoring the peroxide concentration in the chamber can control the concentrating process.

Table 8

	Sterility results (positives / samples)	
	Normal process	New concentrating Process
1 x 400 mm	2 / 2	0 / 2
1 x 350 mm	2 / 2	0 / 2
1 x 300 mm	2 / 2	0 / 2
1 x 250 mm	2 / 2	0 / 2

The pressure and peroxide concentration curves during the concentrating process with 12% peroxide solution by weight are presented in Figure 9. The chamber was set at 45°C. The vaporizer has its own heater and is in communication with the chamber and separated from the chamber with the o-rings. Initially, the heater on the vaporizer was off and the vaporizer was heated to about 45°C due to the heated chamber and air around the vaporizer. As indicated from the pressure and peroxide concentration curves, the majority of molecules vaporized and diffused into the chamber during the first 15 minutes were water. Not much peroxide was vaporized and diffused into the chamber. This is consistent with the data published by Schumb et al., as shown in Table 9, that the concentration of hydrogen peroxide in the vapor phase over a 12% peroxide solution by weight, or 6.7% by mole, is less than 0.5% by mole under our test conditions.

As water and peroxide vaporized from the vaporizer, the vaporizer temperature decreased for more than 10°C. With the valve at the open position while water and peroxide vaporized and diffused into the chamber, more water is removed from the system than the peroxide, and the peroxide concentration left in the vaporizer is increased. As indicated from the graph, the hydrogen peroxide

concentration started to increase after 15 minutes. This indicated that the peroxide solution left in the vaporizer had been concentrated by removing enough water from the vaporizer. The valve was then closed to retain the remaining peroxide vaporized into the sterilizer. The temperature of the vaporizer can then be optionally increased to enhance the vaporization of the remaining peroxide solution left in the vaporizer.

The length of the concentrating process or the time to close the valve can control the final peroxide concentration or the ratio of the peroxide to the water in the chamber. Since water has higher vapor pressure than peroxide at the same temperature, the concentration of peroxide in the vaporizer or the chamber can be increased by increasing the time of the concentrating process or by delaying the time to close the valve. This concentrating process can be conducted with peroxide solution in the chamber and/or in the vaporizer which is in fluid communication with the chamber, and it can be enhanced if the environment, which contains the peroxide solution, is a diffusion-restricted area. Monitoring or determining the concentration of water and/or peroxide in the chamber and/or vaporizer can properly control this concentrating process. It is well known in the prior art that the concentration of peroxide is an important factor to achieve good efficacy for the vapor phase peroxide process. Based on the test results of this invention, it is believed that the ratio of peroxide to water is even more important to control and determine the vapor peroxide sterilization process. By determining the concentrations of peroxide and water in the process and calculating the ratio of peroxide to water, parametric release can be achieved without using the biological indicator. By determining the vapor composition and monitoring the temperature of the peroxide solution, the concentration of the peroxide solution can be determined.

Table 9

Vapor composition (mole fraction H2O2) over hydrogen peroxide water solutions

Temp.	Mole Fraction Hydrogen Peroxide in Liquid								
(°C)	10%	20%	30%	40%	50%	60%	70%	80%	90%
0	0.2%	0.6%	1.5%	3.1%	6.0%	11.2%	20.2%	35.2%	60.0%
10	0.3%	0.8%	1.8%	3.7%	7.0%	12.8%	22.4%	38.1%	62.6%
20	0.3%	0.9%	2.0%	4.1%	7.7%	13.8%	23.8%	39.7%	64.0%
25	0.3%	1.0%	2.2%	4.4%	8.1%	14.4%	24.7%	40.7%	64.8%
30	0.3%	1.0%	2.3%	4.6%	8.5%	15.1%	25.5%	41.7%	65.6%
40	0.4%	1.2%	2.6%	5.2%	9.4%	16.3%	27.2%	43.5%	67.1%
50	0.5%	1.4%	3.0%	5.7%	10.3%	17.5%	28.7%	45.2%	68.4%
60	0.5%	1.5%	3.3%	6.3%	11.1%	18.7%	30.2%	46.8%	69.6%
70	0.6%	1.7%	3.6%	6.8%	12.0%	19.9%	31.6%	48.2%	70.7%
80	0.7%	1.9%	4.0%	7.4%	12.8%	21.0%	32.9%	49.5%	71.6%
90	0.7%	2.1%	4.3%	8.0%	13.6%	22.1%	34.2%	50.8%	72.5%
100	0.8%	2.3%	4.7%	8.5%	14.4%	23.1%	35.4%	51.9%	73.3%

Tables 10A, 10B, and 10C have more detailed information about the peroxide to water ratio in the vapor phase at various temperatures and concentrations by re-calculating the mole fraction data in the Table 9. Since hydrogen peroxide, H_2O_2, has one more oxygen than water, H_2O, the ratio of hydrogen peroxide to water based on the weight is larger than the ratio of hydrogen peroxide to water based on the mole.

Table 10A has the ratios of hydrogen peroxide to water in the vapor phase with 10%, 20% and 30% hydrogen peroxide solutions by mole under various temperatures.

Table 10A

Ratio of peroxide to water in the vapor phase over hydrogen peroxide solutions

Temp. (°C)	10% by mole or 17.3% by weight in solution		20% by mole or 32.1% by weight in solution		30% by mole or 44.7% by weight in solution	
	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight
0	0.0020	0.0038	0.0060	0.0114	0.0152	0.0288
10	0.0030	0.0057	0.0081	0.0152	0.0183	0.0346
20	0.0030	0.0057	0.0091	0.0172	0.0204	0.0385
25	0.0030	0.0057	0.0101	0.0191	0.0225	0.0425
30	0.0030	0.0057	0.0101	0.0191	0.0235	0.0445
40	0.0040	0.0076	0.0121	0.0229	0.0267	0.0504
50	0.0050	0.0095	0.0142	0.0268	0.0309	0.0584
60	0.0050	0.0095	0.0152	0.0288	0.0341	0.0645
70	0.0060	0.0114	0.0173	0.0327	0.0373	0.0705
80	0.0070	0.0133	0.0194	0.0366	0.0417	0.0787
90	0.0070	0.0133	0.0215	0.0405	0.0449	0.0849
100	0.0081	0.0152	0.0235	0.0445	0.0493	0.0932

Table 10B has the hydrogen peroxide to water ratios in the vapor phase with 40%, 50% and 60% hydrogen peroxide solutions by mole.

Table 10B

Ratio of peroxide to water in the vapor phase over hydrogen peroxide solutions

Temp. (°C)	40% by mole or 55.7% by weight in solution		50% by mole or 65.4% by weight in solution		60% by mole or 73.9% by weight in solution	
	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight
0	0.0320	0.0604	0.0638	0.1206	0.1261	0.2382
10	0.0384	0.0726	0.0753	0.1422	0.1468	0.2773
20	0.0428	0.0808	0.0834	0.1576	0.1601	0.3024
25	0.0460	0.0869	0.0881	0.1665	0.1682	0.3178
30	0.0482	0.0911	0.0929	0.1755	0.1779	0.3360
40	0.0549	0.1036	0.1038	0.1960	0.1947	0.3678
50	0.0604	0.1142	0.1148	0.2169	0.2121	0.4007
60	0.0672	0.1270	0.1249	0.2358	0.2300	0.4345
70	0.0730	0.1378	0.1364	0.2576	0.2484	0.4693
80	0.0799	0.1509	0.1468	0.2773	0.2658	0.5021
90	0.0870	0.1643	0.1574	0.2973	0.2837	0.5359
100	0.0929	0.1755	0.1682	0.3178	0.3004	0.5674

Table 10C has the hydrogen peroxide to water ratios in the vapor phase with 70%, 80% and 90% hydrogen peroxide solutions by mole.

Table 10C

Ratio of peroxide to water in the vapor phase over hydrogen peroxide solutions

Temp. (°C)	70% by mole or 81.5% by weight in solution		80% by mole or 88.3% by weight in solution		90% by mole or 94.4% by weight in solution	
	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight	Ratio of peroxide to water in vapor by mole	Ratio of peroxide to water in vapor by weight
0	0.2531	0.4781	0.5432	1.0261	1.5000	2.8333
10	0.2887	0.5452	0.6155	1.1626	1.6738	3.1616
20	0.3123	0.5900	0.6584	1.2436	1.7778	3.3580
25	0.3280	0.6196	0.6863	1.2964	1.8409	3.4773
30	0.3423	0.6465	0.7153	1.3511	1.9070	3.6021
40	0.3736	0.7057	0.7699	1.4543	2.0395	3.8524
50	0.4025	0.7603	0.8248	1.5580	2.1646	4.0886
60	0.4327	0.8173	0.8797	1.6617	2.2895	4.3246
70	0.4620	0.8726	0.9305	1.7576	2.4130	4.5578
80	0.4903	0.9261	0.9802	1.8515	2.5211	4.7621
90	0.5198	0.9818	1.0325	1.9503	2.6364	4.9798
100	0.5480	1.0351	1.0790	2.0381	2.7453	5.1856

By monitoring the concentration (i.e. the peroxide concentration or the ratio of hydrogen peroxide to water) during the sterilization cycle and controlling the timing to close the valve, it should be possible to achieve the long sought goal of parametric release. One could be assured that if the proper concentration was maintained for a sufficient period of time that a particular load of instruments placed within the chamber 30 and sterilized according to the present invention then the process would be sufficiently predictable so as to allow the load to be released for use without further checking with a biological indicator. Typically, such processes

employ a biological indicator in the load, such as with a test load of microorganisms, which is then checked to ensure that sufficient sterilization has been achieved to kill all of the test microorganisms. With parametric release the time consuming process of biological indicators can be skipped.

As described previously, shipping hydrogen peroxide solution with more than 60% by weight is regulated and can be difficult and impractical. One of the goals for this concentrating process is to concentrate the hydrogen peroxide solution in the system from less than 60% by weight to greater than 60% by weight. Therefore, more concentrated hydrogen peroxide can be generated during the process for a more efficacious cycle.

The process may be further enhanced by admitting sufficient hydrogen peroxide into the system so as to force some of the vaporized solution to condense upon the instruments being sterilized within the system. As described above, the solution can be vaporized by admitting it into the system at any pressure above the vapor pressures of water and hydrogen peroxide in the solution and then vaporized by reducing the pressure, or by admitting the solution at a pressure substantially below its vapor pressure whereupon it will start to vaporize thus releasing gas and increasing the pressure. In the second scenario if the pressure is then further reduced by pumping down the system, the concentration of the hydrogen peroxide in the system can be increased. This is especially true if the pressure rises to a level at least above the vapor pressure of hydrogen peroxide thereby limiting further vaporization of hydrogen peroxide from solution and encouraging some of the hydrogen peroxide to condense upon objects such as instruments within the system. Some of the water vapor would likely also condense in such event. By controlling the pressure, excess water vapor would be exhausted from the system and then the condensed solution would re-vaporize. To the extent that such solution had

condensed within diffusion restricted areas the re-vaporization therein would further increase the concentration in those areas to enhance the sterilization efficacy therein. The quantity of solution admitted will primarily determine the pressure rise to initiate such condensation. The process is described in more detail in our co-pending U.S. Application Serial No. 09/223,594 filed December 30, 1999 and entitled "Sterilization of Diffusion-Restricted Area by Re-Vaporizing the Condensed Vapor", which is incorporated herein by reference.

A typical cycle might comprise placing a load of instruments (not shown) within a CSR wrapped tray within the chamber 30 and then drawing a vacuum on the chamber 30 with the pump 32 down to below 1 torr or about 0.3 torr. An electromagnetic field applied to the chamber 30 at such time tends to drive any remaining water into the vapor or plasma stage so that the pump 32 can remove it. The pump 32 can be cycled or merely run continuously with the valve 34 controlling the vacuum process. Fresh dry air may be admitted to the chamber 30 raising the pressure back to atmosphere. Preferably the hydrogen peroxide solution, preferably a 59% hydrogen peroxide solution by weight, is admitted to the vaporizer 36 at atmospheric pressure and then the pump 32 exhausts the chamber 30 to a level at which the solution begins to vaporize. A monitor 100 for hydrogen peroxide vapor and monitor 102 (see FIG. 6) for water vapor in connection with an automated control system 104 can be employed to optimize the pressure conditions to enhance the initial vaporization and exhaust of water vapor. After the solution is sufficiently concentrated the temperature of the vaporizer 36 can be increased to vaporize the remaining solution. The valve 32 is closed to isolate the chamber 30 and the vaporized hydrogen peroxide solution is allowed to diffuse throughout the chamber to contact the instruments. Additional dry air or other gas can be admitted at this time to help push the sterilizing vapors into diffusion restricted areas, with the chamber 30 then further exhausted to resume a vacuum in the range of 2 to 10 torr.

Additional admissions of air and vacuum can be employed, especially in connection with additional admission and concentration of hydrogen peroxide solutions. After the hydrogen peroxide vapors have diffused throughout the chamber for a sufficient time an electromagnetic field may be applied to drive the vapor into the plasma stage and effect further sterilization. When the field is removed the activated species formed from the hydrogen peroxide recombine as water and oxygen, leaving little residual hydrogen peroxide. The chamber can be raised to atmospheric pressure and the load removed.

It should be noted that the present invention is not limited to only those embodiments described in the Detailed Description. Any embodiment which retains the spirit of the present invention should be considered to be within its scope. However, the invention is only limited by the scope of the following claims.

WHAT IS CLAIMED IS:

1. A method of furnishing concentrated hydrogen peroxide vapor to an article comprising the steps of:

placing the article into a chamber containing an inner atmosphere;

placing a solution comprising hydrogen peroxide and water into fluid communication with the chamber, the solution having a ratio of hydrogen peroxide to water;

vaporizing the solution in the inner atmosphere to form water vapor and hydrogen peroxide vapor;

selectively drawing water vapor from the chamber to increase a ratio of hydrogen peroxide to water in the chamber; and

contacting the article with the hydrogen peroxide vapor.

2. A method according to claim 1 wherein the ratio of hydrogen peroxide vapor to water vapor after the step of selectively drawing water vapor from the chamber exceeds the ratio of hydrogen peroxide to water in said solution.

3. A method according to claim 1 wherein the ratio of hydrogen peroxide to water, by weight, after the step of selectively drawing water vapor from the chamber exceeds 3 to 1.

4. A method according to claim 3 wherein the ratio of hydrogen peroxide to water in said solution, by weight, is less than 3 to 1.

5. A method according to claim 3 wherein the ratio of hydrogen peroxide to water in said solution, by weight, is less than 3:2.

6. A method according to claim 3 wherein the ratio of hydrogen peroxide to water, by weight, after the step of selectively drawing water vapor from the chamber exceeds 4 to 1.

7. A method according to claim 1 wherein the step of selectively drawing water vapor from the chamber comprises placing said solution within a diffusion restricted environment in fluid communication with the chamber during the step of vaporizing the solution.

8. A method according to claim 7 wherein the diffusion restricted environment is more diffusion restricted during the step of selectively drawing water vapor from the chamber than during a portion of the step of vaporizing the solution without selectively drawing water vapor from the chamber.

9. A method according to claim 7 wherein the water vapor is drawn from the chamber through one or more exhaust ports and wherein the one or more exhaust ports are physically remote from the diffusion restriction.

10. A method according to claim 1 wherein the step of selectively drawing water vapor from the chamber comprises the steps of controlling the temperature and pressure of the solution during the step of vaporizing the solution to enhance vaporization of the water from solution versus vaporization of hydrogen peroxide and extracting at least a portion of the water vapor from the chamber.

11. A method according to claim 1 wherein the step of selectively drawing water vapor from the chamber comprises the steps of maintaining the solution at a pressure below the vapor pressure of the water in the solution and above the vapor pressure of the hydrogen peroxide in the solution.

12. A method according to claim 1 wherein the solution is vaporized by pumping a portion of the atmosphere out of the chamber to lower the pressure of the chamber at a rate selected to control removal of the water and hydrogen peroxide from the solution so as to concentrate the hydrogen peroxide remaining in the chamber.

13. A method according to claim 1 wherein the temperature of the solution during the vaporizing step is held below the temperature of the atmosphere in the chamber whereby to increase the vapor pressure of the water in the solution relative to the hydrogen peroxide in the solution whereby to enhance vaporization of the water from the solution in preference to vaporizing the hydrogen peroxide from the solution.

14. A method according to claim 13 wherein the temperature of the atmosphere in the chamber is above room temperature and the temperature of the solution during the vaporizing step is at least 10° C below the temperature of the atmosphere in the chamber.

15. A method according to claim 13 wherein the solution is vaporized in a vaporizer which is in fluid communication with the chamber and wherein the vaporizer is thermally isolated from the chamber.

16. A method according to claim 1 and further comprising the steps of controlling the temperature and pressure of the solution during a least a first portion of the vaporizing step so as to selectively vaporize water from the solution and concentrate hydrogen peroxide therein to form a concentrated solution and during a

second portion of the vaporizing step raising the temperature of the concentrated solution and vaporizing the concentrated solution.

17. A method according to claim 1 and further comprising the steps of controlling the temperature and pressure of the solution during at least a first portion of the vaporizing step so as to selectively vaporize water from the solution and concentrate hydrogen peroxide therein to form a concentrated solution and during a second portion of the vaporizing step not withdrawing atmosphere from the chamber.

18. A method according to claim 1 and further comprising the step of drying the chamber prior to the step of vaporizing the solution.

19. A method according to claim 18 wherein the step of drying the chamber comprises pumping a portion of the atmosphere out of the chamber.

20. A method according to claim 18 wherein the step of drying the chamber comprises applying energy to excite molecules of liquid water within the chamber into the gaseous or plasma state of matter and pumping a portion of the atmosphere out of the chamber.

21. A method according to claim 1 wherein the step of contacting the article with the hydrogen peroxide vapor is limited to less than one hour and if the article were to have a straight round lumen having two open ends, a diameter of 1mm and a length of 250mm with 10^6 viable spores of B. Stearothermophilus located within the lumen at a midpoint thereof, all of the spores would be killed.

22. A method according to claim 1 wherein the solution comprises

peracetic acid.

23. A method according to claim 1 wherein the step of placing the solution comprising hydrogen peroxide and water into fluid communication with the chamber occurs at atmospheric pressure.

24. A method according to claim 1 wherein the step of placing the solution comprising hydrogen peroxide and water into fluid communication with the chamber occurs at the vapor pressure of said solution.

25. A method according to claim 1 wherein the step of placing the solution comprising hydrogen peroxide and water into fluid communication with the chamber occurs below the vapor pressure of said solution.

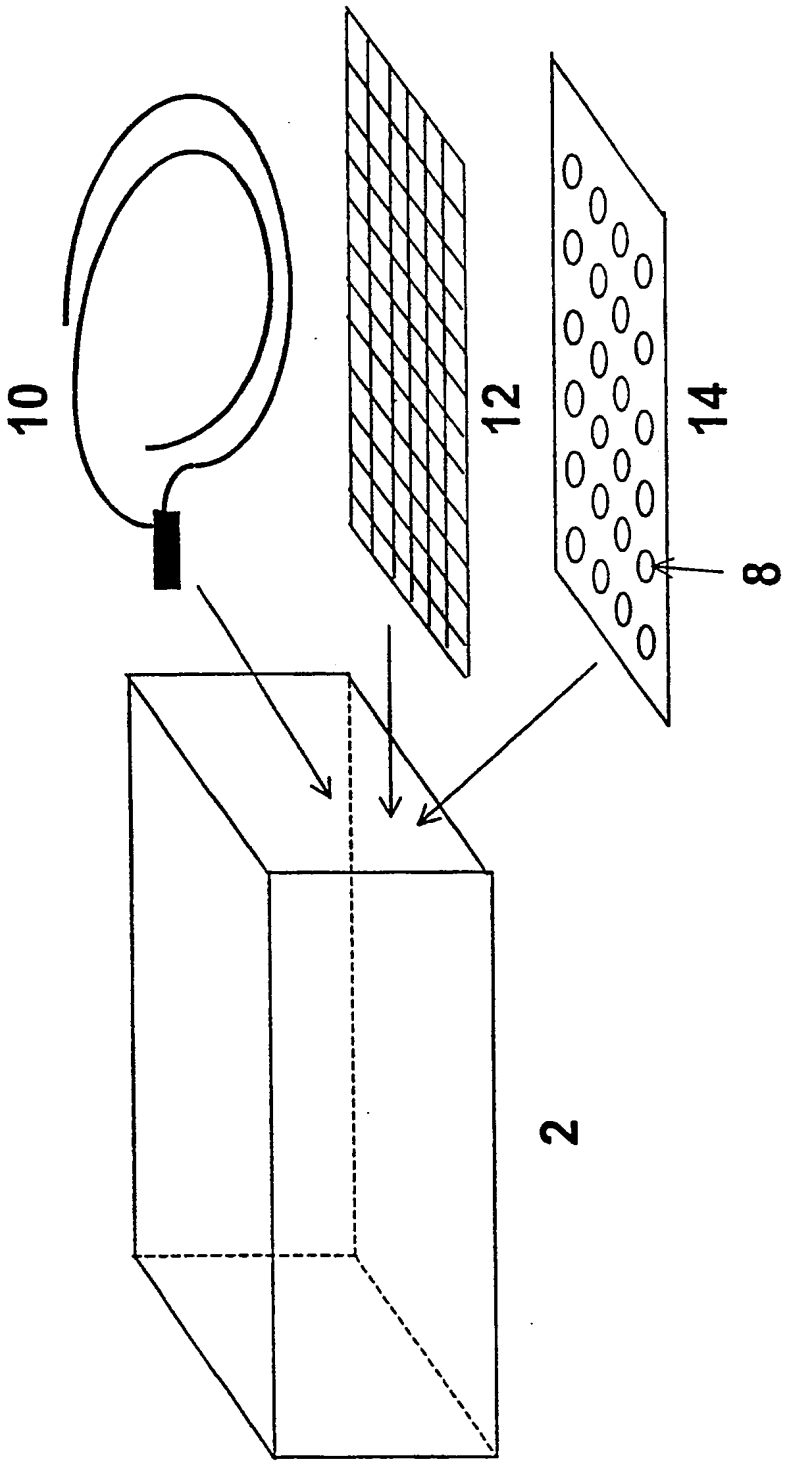

Figure 1

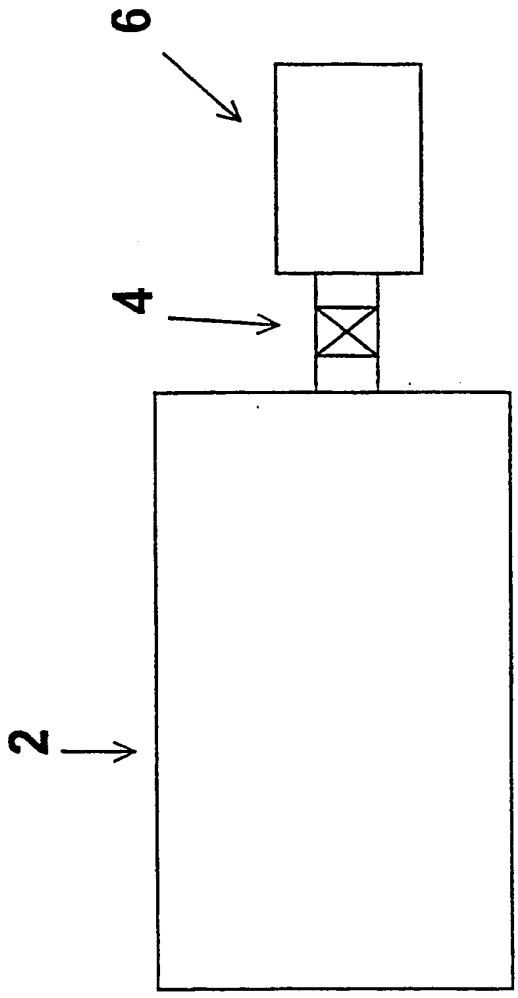

Figure 2

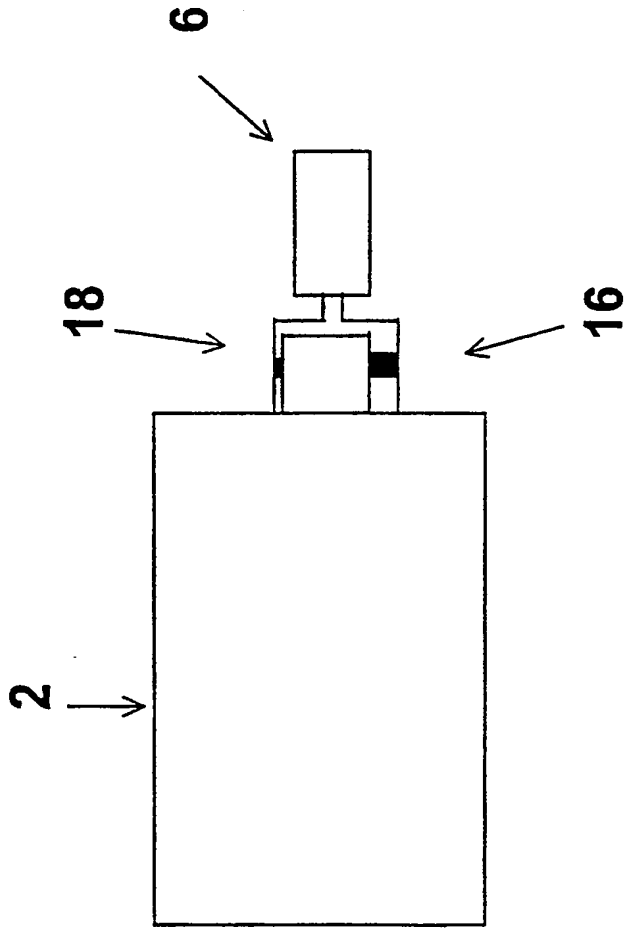

Figure 3

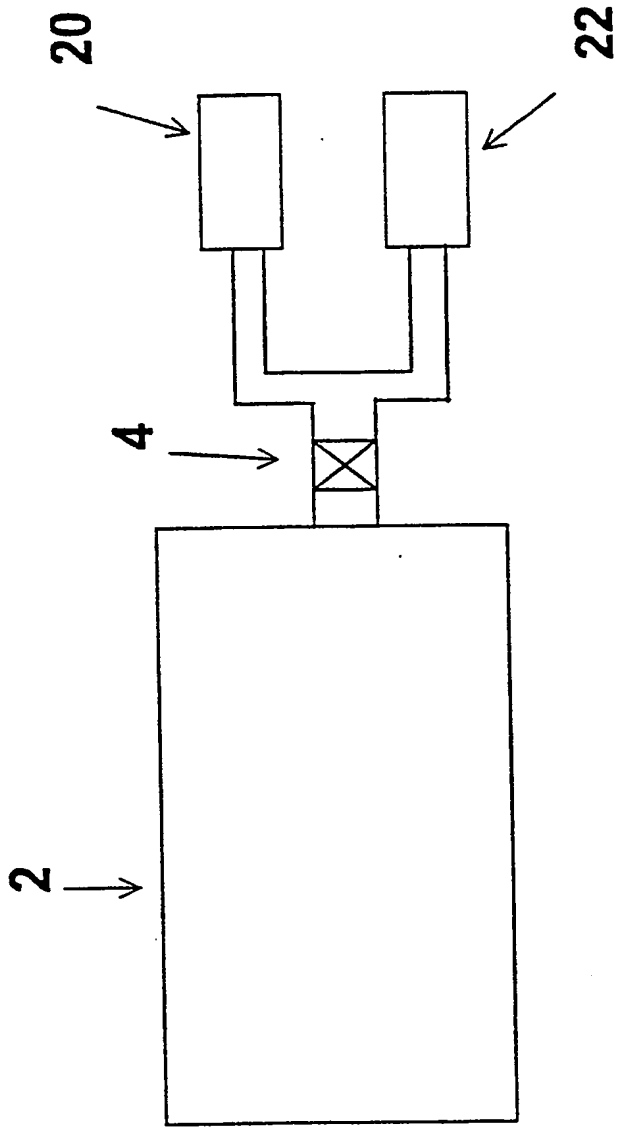

Figure 4

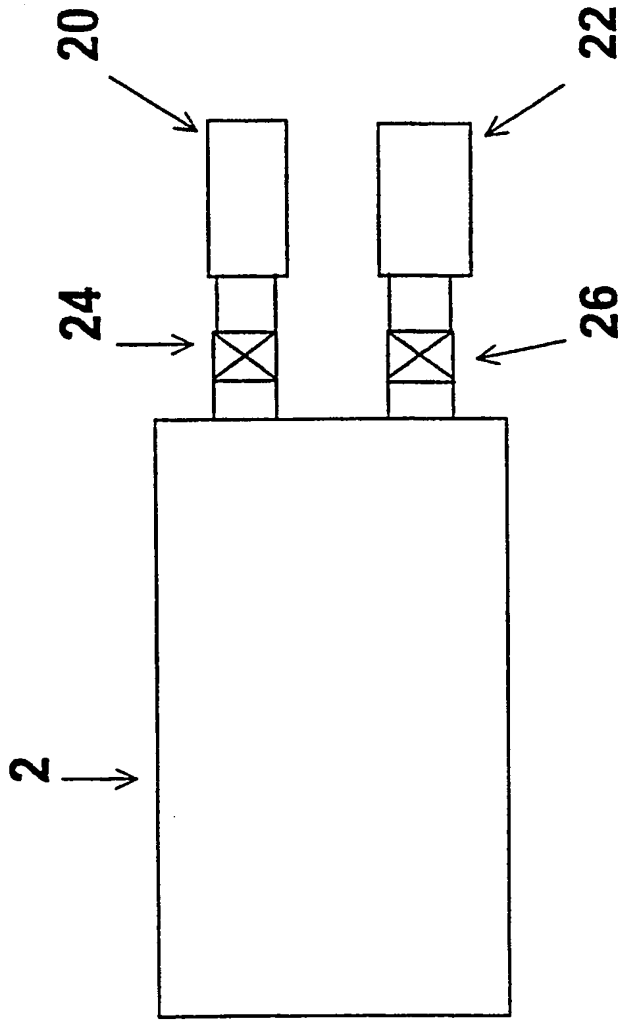

Figure 5

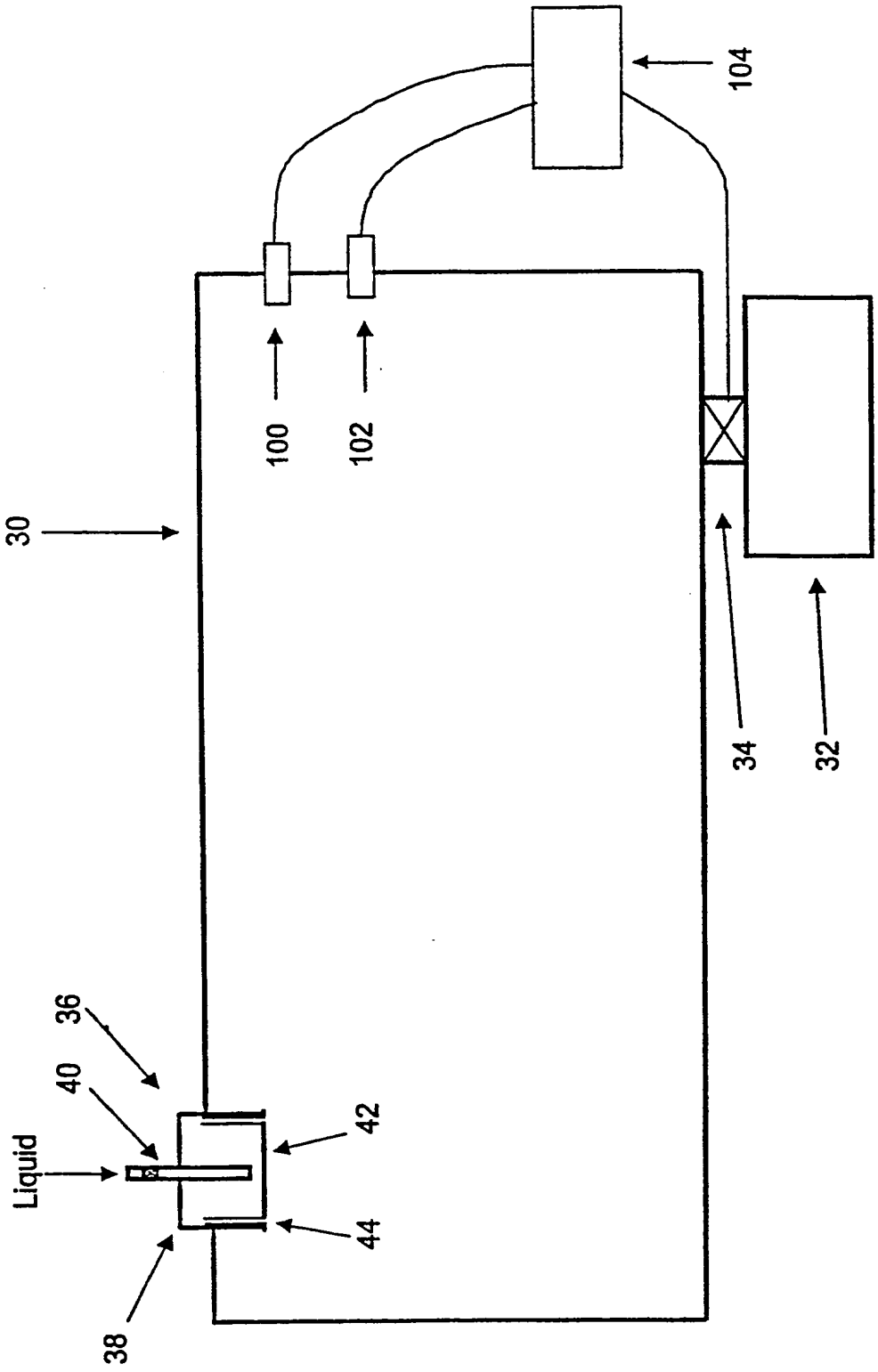

Figure 6

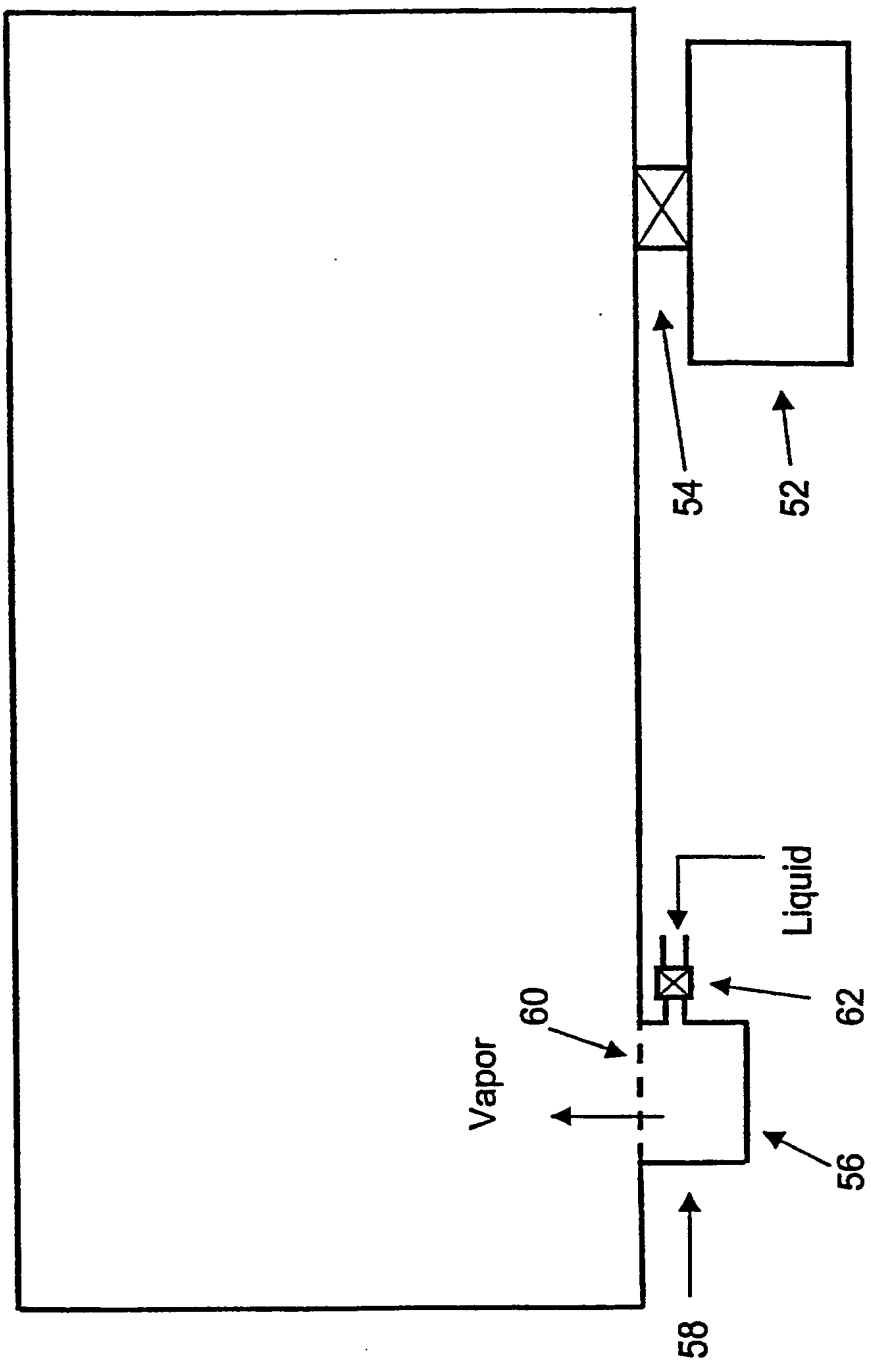

Figure 7

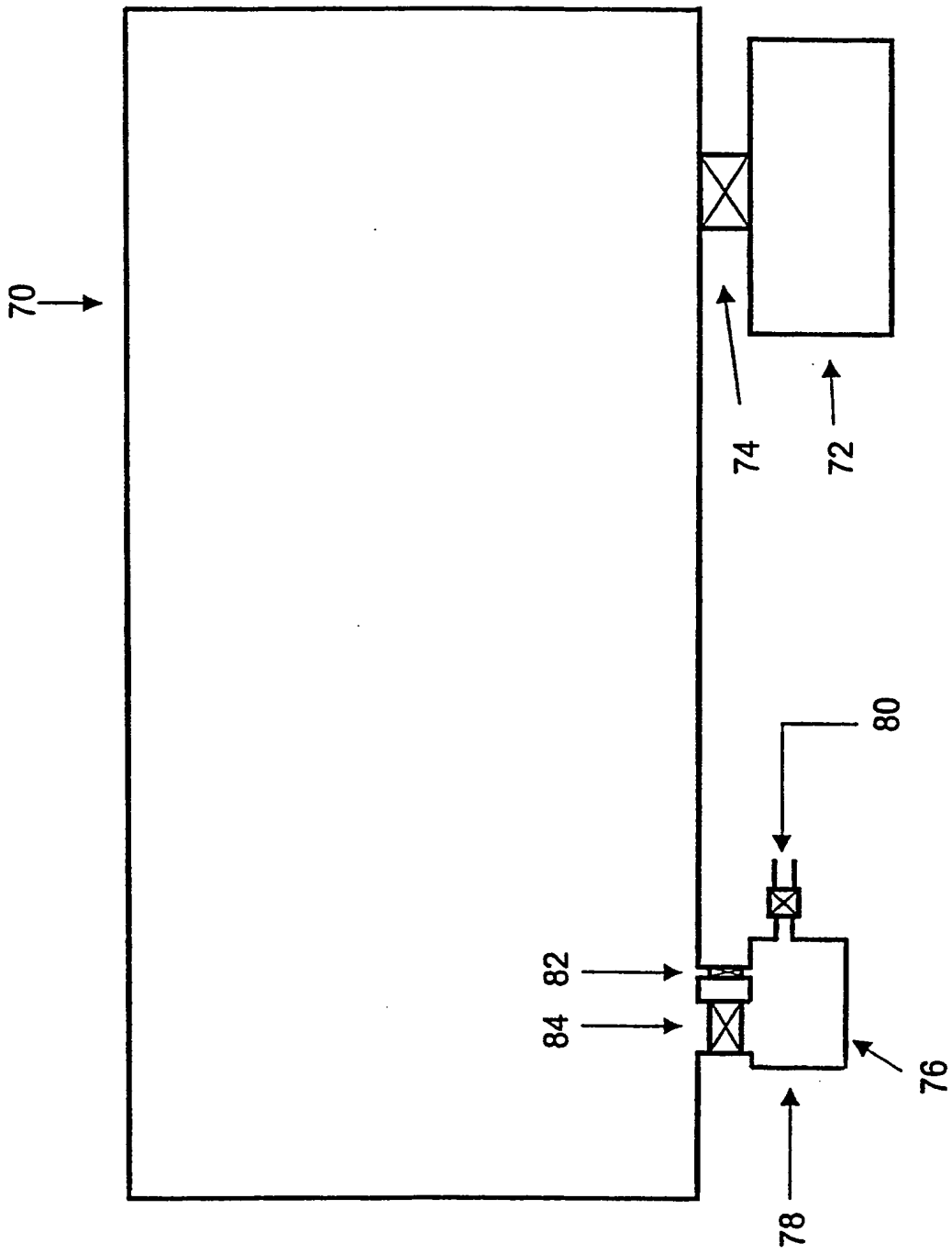

Figure 8

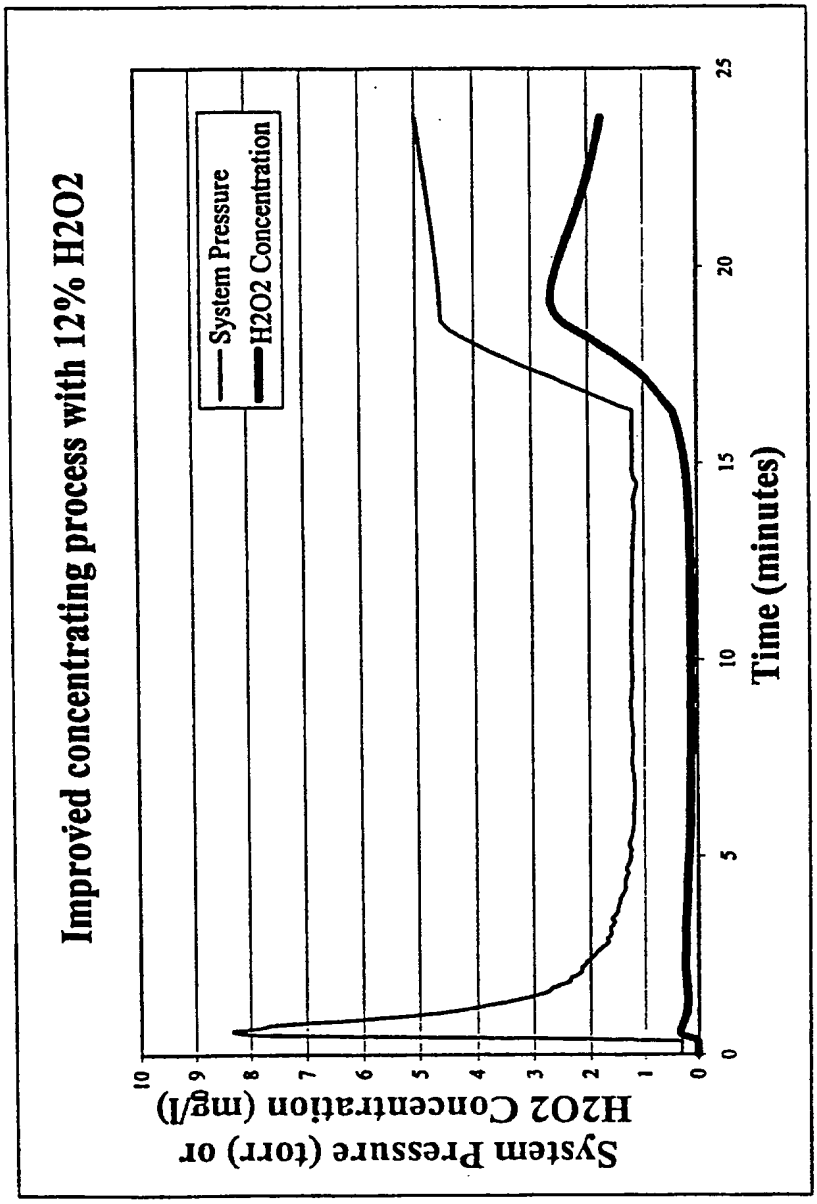
Improved concentrating process with 12% H2O2
System Pressure
H2O2 Concentration
System Pressure (torr) or
H2O2 Concentration (mg/l)
Time (minutes)
0
1
2
3
4
5
6
7
8
9
10
0
5
10
15
20
25

Figure 9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/31140

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61L 2/20
US CL :422/28,33

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 422/28,33

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

NONE

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

NONE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y ---- A	US 4,744,951 A (CUMMINGS et al) 17 May 1988 (17.05.88), see entire document.	1-7,10-13, 15-19,21, 25 ---------- 20,22 ---------- 8,9,14,23, 24
Y	US 5,389,336 A (CHILDERS) 14 February 1995 (14.02.95), see abstract.	22
Y	US 5,656,238 A (SPENCER et al) 12 August 1997 (12.08.97), see abstract.	20

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 12 MARCH 2000	Date of mailing of the international search report 04 APR 2000
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